Exhibit*1
P-10926.00 LW091

Medtronic

INVENTION DISCLOSURE FORM

Completing this form is one of the first steps taken in obtaining a patent protection. Please carefully consider and thoroughly answer all the questions in this form, as doing so will ensure your invention receives a fair and full hearing when the European Patent Review Board convenes to determine whether patent protection should be sought for your invention. It is generally best to complete the form early in the invention process. Additional information derived from experiments or further reduction to practice can always be submitted in supplements to the original disclosure.

Except in the case of some chemical inventions, there is no legal or other requirement that your invention actually be reduced to practice before the disclosure form can be submitted or even before a patent application can be filed. Before starting to complete the form, it is generally a good idea to assemble and have on hand drawings and technical descriptions of your invention, as well as any copies of pertinent background articles, books, advertisements, brochures or catalogs that may be available. Make sure you attach copies of those materials to the form before sending it in. When completed, have your manager sign the form and forward the original to Tom Woods at the Bakken Research Center in the Netherlands, Mail Stop IR-51. You should keep a complete copy of the signed and completed disclosure form for your own records.

1. **Full names and complete home addresses of all Inventor(s)/Contributor(s):**

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2. Title of your Invention:

Method for facilitating lead delivery into coronary sinus and coronary veins using sensors.

3. Briefly describe your invention and how it relates to your work.

A physiological signal is measured at several places on the lead delivery system. These signals contain information that can be related to the anatomical position of the sensors and facilitate delivery of the lead to the right location.
This continues to be a project at the BRC.

4. What problem is solved by your invention? How does your invention solve that problem?

For a number of patients pacing of the left ventricle provides the optimum therapy. Lead delivery into the coronary sinus and peripheral coronary veins is one of the possibilities to approach this position. However, transvenous lead delivery to that location is very difficult for a number of reasons. One of these is that the coronary sinus cannot be found with X-ray only. Consequently, the lead

implantation has a large range making it impossible to plan the OR time and the success rate is low.
We have solved this problem by using sensors on the delivery system. The information contained in the sensed signals is related to the anatomic position. This is combined with a device that presents these data in a form that it can be used as a navigational tool.

5. If your invention relates to a device, attach or provide drawings that show all essential or important components of the invention. Label the components in the drawings.

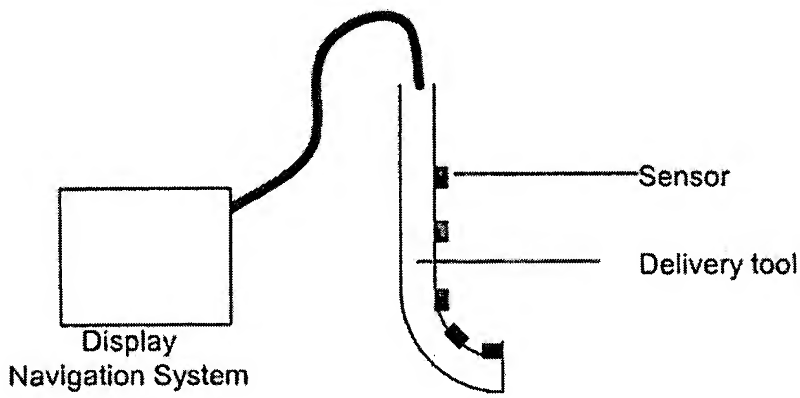

Figure 1. Schematic drawing of the device.

A number of sensors are mounted on several spots on the delivery tool.
The sensors might be temperature sensors (for example thermocouples or thermistors); oxygen sensors (for example optical or electrochemical); pressure sensors (for example optical or piezo-electrical); electrical sensors (metal electrodes) or basically any other sensor or combination of sensors that measure a physiological signal in the blood/tissue.

This tool can have various fixed forms specific for a certain anatomy, or it can be a flexible tool that can be manipulated by the operator to have any desired shape, some details are given in the figure below.

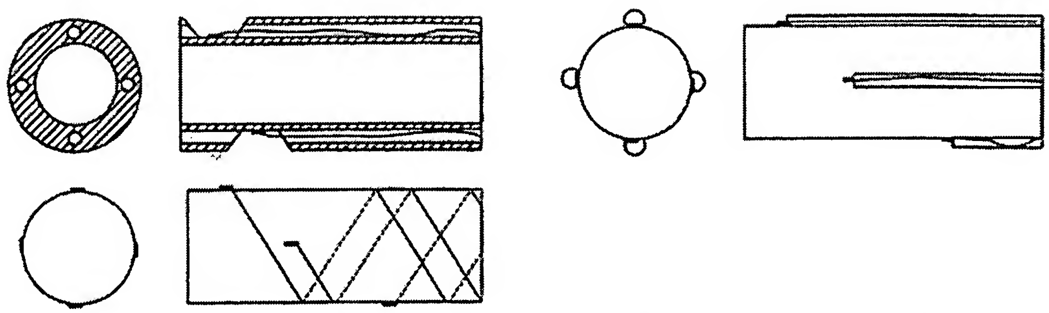

Figure 2 <u>TopLeft:</u> Multilumen tube with sensors in the lumen and windows to the outside at various positions. <u>TopRight:</u> Central catheter with small tubes containing the sensors attached to the outside. <u>Bottom:</u> sensors on the outside of a catheter.

This can be integrated with a steerable guiding catheter like the 10600.
It can also be a passive tube that becomes steerable by a stylet or by a steerable catheter in the central lumen.

The tool can have a special shape meant to increase the signals. For example a curve or a tapered tip that increases the pressure signal to be measured when entering or approaching the coronary sinus.

6. **If your invention relates to a method[1], please provide one or more flow charts showing the individual steps of your invention. Be sure to include details concerning the most important steps of the method. Include drawings or written descriptions of or references to any important equipment used in the method. For example, important components, equipment or machinery employed in an important step should be described, the general specifications of the equipment listed, and pertinent information included concerning how the component or equipment is used in the step.**

The focus in the description of the method will be on the use of temperature recordings, although other signals (or combinations) might also be used.

The temperature of the blood coming from the coronary sinus differs from the blood in the right atrium. An indication for this is given by Stewart[1]. Animal experiments (dog) in the course of this project indicate that there is a temperature gradient of about 1 °C extending approximately one cm out of the coronary sinus ostium. This invention is based on the fact that such a difference distinguishing the target area from the other areas exists.

[1] If your invention relates to both a device and a method, please include the information requested for both.

Suppose the method involves the use of Loca Lisa and temperature recordings. In that case a temperature anatomical map of the heart can be made by moving the catheter around while continuously recording position and temperature. While doing this the map gets more complete and one can see where to go to find the coronary sinus (maximum temperature).

If the LocaLisa system is not available (most likely it is not) then in the worst case we could say that the temperature in the coronary sinus is higher then in the right atrium but no gradient extends outside of the ostium. In that case this device still helps in confirming that the coronary sinus is reached based on the temperature change. It is not always easy to see this on the basis of X-ray only. However, it would not help in finding the ostium.

If there is a gradient in temperature as described above in dogs then we could use that information to find the ostium. To measure this it might be advantageous to have multiple temperature sensors on the catheter. Thermocouples would be a good choice because they are cheap. The recording could be multiplexed so only one recorder is necessary. Positions could be at the tip, and then 5 additional sensors each two millimeter apart and a last one 1 cm apart.

The macroscopic navigation will still be done with X-ray. As soon as the tip of the catheter gets in the range of the gradient that can take over. The principle is sketched in the figure below.

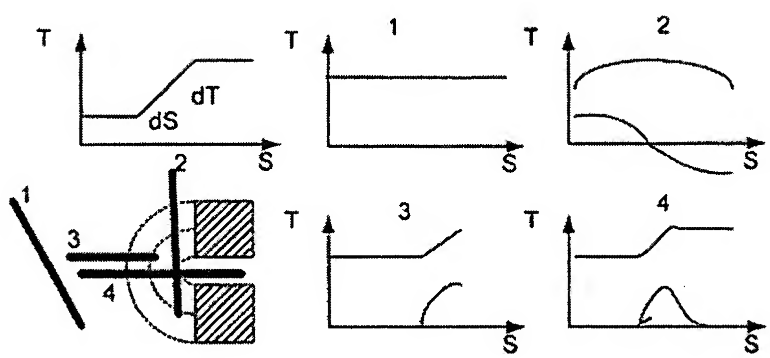

Figure 3 Temperature situation around the ostium of the coronary sinus, some typical positions of the catheter in that area (1,2,3,4) and the temperature as a function of position and derivative that can distinguish between those positions and that are the basis to provide directional information.

The next step is if a temperature anatomical map exists that is approximately the same for all patients, or that contains particular distinguishing features that are

the same in all patients. This can then be used in a similar way as described abive.

A problem arises when the sensor readings fit on this map in multiple ways, that is the sensor information does not determine the position of the catheter in a unique way.

This could be solved by feeding the information from the X-ray image into the delivery system. With image recognition the position of the catheter can be derived from the image. If the camera angle is also known then this information can be used to determine the position of the catheter in the temperature map and the navigational directions can continue.

Another way is if the shape of the delivery tool is known from the position of the buttons on the grip that are used by the physician. If the position at the introduction sheet is kept fixed this can be used to do the same.

It could be possible to just provide the catheter with the sensors and make it compatible with equipment commonly available in the cathlab (monitors, amplifiers, signal acquisition).

The system could "talk", making statements like "advance catheter", "turn counter clockwise" and "congratulations, you have succeeded to enter the coronary sinus" (replacing the last message by "you are in the coronary sinus" after the same operator has used it for a couple of times).
The system can feature a red light / green light type of feedback to the physician.
A monitoring system could display the recorded signals as they are. The signals might also be processed and then be displayed for example gradients, phase angle relative to cardiac cycle or number of signal characteristics in one period.
A separate part of this monitoring system automatically displays directional information calculated on the basis of the recorded signals. The right direction is known from an experimentally established relation between the physiological signals and the anatomy that is valid in all patients. For example it can be towards maximal temperature.
More in general, the morphology of the recorded signals like frequency content and time domain content can be used to derive navigational information which is displayed in a convenient form.

A possible method to deliver leads to the Coronary Sinus with this device could be:
A delivery tool equiped with sensors and a display showing navigational information is used to find the ostium of the coronary sinus. Once this position is found another tool is brought in, for example a guiding catheter that can move over the sensor tool. Once this guiding catheter is positioned in the coronary sinus the delivery tool can be removed and lead delivery can continue in various ways. The exact method depends on the kind of catheter used. For example the

sensors might be integrated on the delivery catheter, like described in the previous chapter

To increase the signal gradient or, more in general, to increase the navigational information present in the signal, some special procedures might be carried out during the implant.
For example chemicals temporarily affecting viscosity or vaso dilation may be used.
Temporarily occluding the vena cava can increase the signal to noise ratio and navigational content as well.
Injecting fluids with different properties then the blood in the Coronary Sinus.

7. Describe as many mechanically, chemically or electrically different embodiments of the invention as you can, even if you would not use them in a product. Put yourself in the shoes of a competitor who first reads a patent covering only the primary embodiment of your invention, and who then proceeds to design around the patent. This important exercise can permit our competitors' design around efforts to be anticipated.

The navigational display system is valid with any type of other sensor, for example PH, flow, lactate. It can also be used with combinations of sensors.

In the case of other sensors the signal enhancement as described in the method might be achieved in other ways. Injecting something in the right ventricle will return into the right atrium through the coronary sinus just before it will also return also through the vena cava. This might also be used to increase the signal.

The delivery method as described in the previous paragraph can be done in a number of different ways, all having the same principle of having a tool with a number of sensors leading the way and then continuing with other tools.
For example the sensor could be integrated with the delivery catheter.

8. List all the problems you can think of that are known to those who work in your field of endeavor, and that your invention may or may not provide a solution to. Please pay special attention to listing these problems, as they may play a important role in determining your invention's patentability.

Current coronary sinus lead implantation times have a large range and the chance of success is low. Mean cause is that the coronary sinus can't be found. This invention will solve that.

The type of navigation described in this invention is not only limited to application for left heart leads. It might also be used in other procedures, for example

ablation of the pulmonary veins. A catheter as disclosed in US 6,325,797 B1 is a good example. The sensors could be incorporated on the guide wire, the sheath, the mapping device or the locating device described in that patent.

9. List __ ie advantages that the various embodiments of your invention are capable of providing. Think of and write down below as many different advantages of your invention as possible. Please pay special attention to the advantages of your invention, as they may also play a important role in determining the patentability of your invention.

No radiation required.

Multiple sensors allow the reading of various gradients simultaneously.

The system automatically provides navigational information, the doctor does not have to derive this from the recorded signals himself.

The system talks to the physician, giving him the opportunity to focus on his hands and listen.

This tool will bring down the lead implantation time, increase the success rate and allow anyone to deliver a lead into the Coronary Sinus.

The principle can also be used in other procedures where something has to be positioned inside the human body, for example when ablating the pulmonary veins.

The fact that the sensors are there on the delivery system makes it possible to use them in the rest of the implant procedure (details will be disclosed in another invention disclosure)

10. List all important structural, chemical, electrical or other physical characteristics, components or distinguishing features of the various embodiments of your invention. Please pay special attention to these characteristics, components and features, as they may play a important role in determining the patentability of your invention.

There are multiple sensors along the length of the guiding system.

The system automatically provides navigational information as opposed to just providing the recorded sensor signals.

11. How have others addressed the problems solved by your invention? List all pertinent books, articles, devices, products or other background materials you know of that relate to your invention, putting a special

emphasis on those materials or "prior art" that are closest to your invention. Whenever possible, attach to this form copies of the prior art you believe is most pertinent to your invention. Remember that the term "prior art" is not restricted to patents only, but includes other printed publications such as technical papers, manuals, advertisements and sales brochures, as well as previously manufactured products or components.

The general problem of pacing the left side of the heart is solved in other ways than approaching it via the coronary veins. For example minimal invasive epicardial or transvenous transseptal.

A catheter which is used to accurately measure temperatures in the human body is described by Hiles[2].

The measurement of blood pressure inside the body is not new. There are numerous vendors of pressure tip catheters and there are numerous publications of pressure measurements using these sensors, including measurements in the coronary sinus and veins[3,4].

The fact that the pressure has an extra peak in the coronary sinus compared to the right atrium and that this can be used for navigation is mentioned already by others[4].

Millar describes a catheter allowing the measurement of a pressure differential between two places on the catheter[5].

Millar also describes a system to attach various sensors on a wire allowing them to move over the wire[6].

Radi Medical Systems has patents on mounting a pressure sensor on a guide wire[7,8].

A previous prior art search was done when this idea was originally proposed with the focus on pressure

12. The invention is described on pages 1-2, 62-65 of Lab Notebook No. ıd pages 67, 70-74, 85, 88-93, 95-100 of Lab Notebook No. Please attach copies of pertinent pages from your lab notebook to this form.

13. When was a device built which included the invention?
December

Who built it?

Viktor Duysens

Where is it?
Office Rogier Receveur

Who has supporting documents?
Rogier Receveur

Who witnessed tests?
Rogier Receveur
Nico Lokhoff
Koen Michels
Olaf Eick
A draft of the report with the results is attached to this invention disclosure.

When and where?
December 11 2001, Medical Center Maastricht
[redacted], Medical Center Maastricht

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june 21 [redacted]
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june 21 [redacted]
Vincent Larik — **Date**

June 21, [redacted]
Nico Lokhoff — **Date**

Ron van der Kruk | **Date** 25 June [redacted]

John Feron | **Date** 21. June [redacted]

Victor Duysens | **Date** 21 June [redacted]

15. Manager's Comments

How important is this invention to your products, plans or goals? Why?

CONSISTENT & EFFICIENT IMPLANT PROCEDURES OF LV lead placement.

Manager's Signature____________________ **Date** 26 jun [redacted]

(Manager: Please forward the completed form to Tom Woods at the Bakken Research Center in the Netherlands, Mail Stop IR-51, upon completion of your review.)

Reference List

1. Stewart,J.T. *et al.* Left ventricular energetics: heat production by the human heart. *Cardiovasc. Res.* 27, 1024-1032 (1993).

2. Hiles,M.C., Bourland,J.D., Wessale,J.L., Geddes,L.A. & Voorhees,W.D. Detection of ventricular tachycardia and fibrillation using coronary sinus blood temperature: a feasibility study. *Pacing Clin. Electrophysiol.* 16, 2266-2278 (1993).

3. Armour,J.A. & Klassen,G.A. Epicardial coronary venous pressure. *Can. J. Physiol Pharmacol.* 59, 1250-1259 (1981).

4. Huang,C.H., Lai,S.T. & Weng,Z.C. The pressure waveform of coronary sinus in human hearts. *Zhonghua Yi. Xue. Za Zhi. (Taipei)* 64, 147-152 [redacted]

5. Millar,H.D. Single sensor pressure differential device. Millar Instruments Inc. 186,898(US 4,901,731). 1990.
Ref Type: Patent

6. Millar,H.D. Method and assembly for introducing multiple catheters into a biological vessel. Millar Instruments Inc. 931,273(US 4,771,782). 1988.
Ref Type: Patent

7. Tenerz,L. & Akerfeldt,D. Sensor guide construction and use thereof. Radi Medical Systems AB. 728,142(US 5,226,423). 1993.
Ref Type: Patent

8. Tenerz,L., Hammarstrom,O. & Smith,L. Pressure sensor and guide wire assembly for biolgical pressure measurements. Radi Medical Systems AB. 09/547,733(US 6,167,763 B1). [redacted]
Ref Type: Patent

Research Report

Title:	Coronary Sinus Lead Delivery System using Miniature Temperature Sensors as a means for Navigation.
Department:	Advanced Concepts

Sign off

	Name	Function	Signature	Date
Prepared By:	Rogier Receveur	Senior Design Engineer		
Approved By:	Vincent Larik	Manager Advanced Concepts		
Approved By:	Jo Bleijlevens	Senior Quality Design Engineer		

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Revision overview

Revision	Description
A	First Issue

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SUMMARY

Context

Treating patients with Heart Failure requires synchronization of both ventricles. The traditional transcutenous transvenous approach of the left heart is very difficult. The advanced concepts department of the Bakken Research Center takes part in a project called biomedical sensors for acute medical use. The focus of this project is to develop a lead delivery system (especially for Coronary Sinus leads) with help of sensors, in this case temperature sensors.

Goal

Check if blood temperature contains information that can be correlated to the position and hence can be used as a navigation system.

Method

A literature study was done to find the previous work. A standard ablation catheter with a thermocouple at the tip and a custom catheter containing three thermocouples at different positions from the tip electrode where used. The tip electrode allows continuous recording of the position of the catheter with the Loca Lisa system. An animal experiment was performed after approval of the protocol by the animal ethical committee and two additional animal experiments were done in collaboration with other groups.

Results

Temperature, position and ECG were simultaneously recorded while removing the catheter from the Coronary Sinus in a dog. Temperature only was recorded in and around the coronary sinus of a calf. Temperature and position were recorded in a dog. This data is investigated in several ways to check for a relation between position and temperature.

Conclusion

These measurements show that there is a temperature difference between the blood in the coronary sinus and the blood in the atrium of approximately 1°C. The spatial extent of the gradient is estimated at approximately 0.5cm around the ostium.

Main improvement for a follow up would be a higher sample rate of the temperature and synchronization with the ECG.

It might be possible to collect data from humans from standard ablation procedures with catheters with thermocouples, if temperature data can be recorded.

INTRODUCTION

Treating patients with Heart Failure requires synchronization of both ventricles. The method that is currently used in clinics is the conventional subclavian approach to the right atrium (RA) and from there to the coronary sinus (CS) and further into coronary veins (see Figure 4). However, this approach is very difficult with only a few specialists performing these operations. The lead has to overcome four 90 degrees angles in this trajectory. The Insync III LV implant time range was 35 to 345 minutes (n=115, median 107)[1]. Implant success rate was 96%. These ranges do not allow good OR planning, increase risk for the patient and raise costs.
Advances in the design of sensors allow acute measurements at the distal end of implant systems as small as 2Fr.[2,3]. Maybe temperature recordings could be used to lead the way to the CS.

[redacted] the advanced concepts department of the Bakken Research Center took part in a project called biomedical sensors for acute medical use[4]. The focus of this project was to develop a lead delivery system (especially for Coronary Sinus leads) with help of sensors, in that case pressure sensors[5]. After discussing those results in the CRM research meeting and with the CRM sensor group it was decided that temperature or pO2 are more appropriate signals to use for navigation purposes in the heart. The project is continued [redacted] with a focus on these signals. This report describes the results of the temperature measurements that were done.

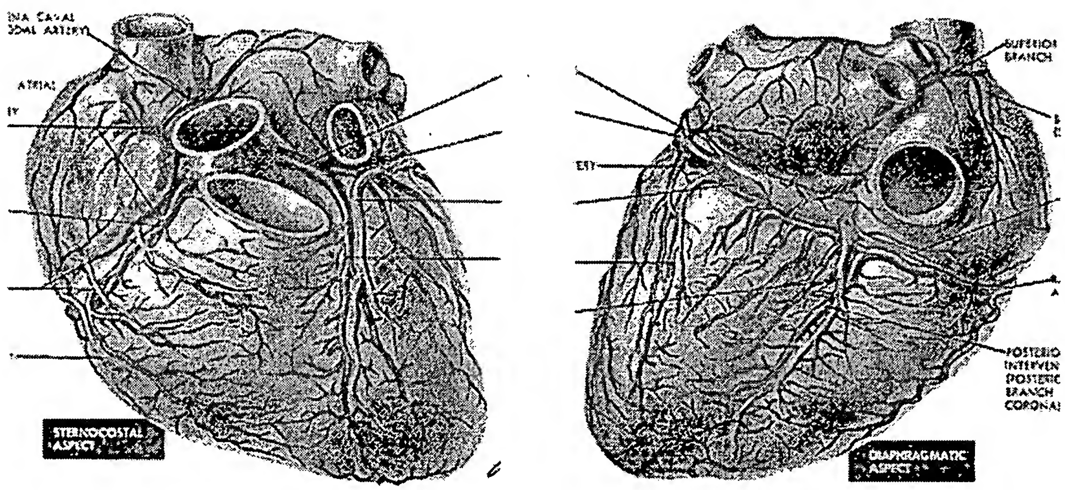


Figure 4 Human Coronary Veins. The coronary sinus has to be entered from the right atrium.

PREVIOUS WORK AND THEORY

To get an idea if knowledge of the temperature can help in finding the CS we have investigated what has already been measured in this area and some simulations were done at the MBC in Minneapolis (Cushing Hamlen).

In an article about left ventricular energetics in which temperatures and temperature differences are measured with thermodilution catheteters the temperature difference between the aorta and coronary sinus is reported to be 0.18 (0.05) °C[6]. Depending on how one reasons this can be either an upper or a lower limit for the temperature difference between right atrial and coronary sinus blood. Either the blood in the aorta is colder then in the right atrium because it came from the lungs were it was cooled, or it is warmer because the heart muscle produces a lot of heat and warms the blood.

Whatever the real situation is, this value was taken as an indication for the kind of temperature differences that might be expected.

Another article describes the detection of arrhythmias from measurement of the temperature in the coronary sinus[7]. Although no value for the temperature difference with the atrial blood can be found in this article it describes the type of catheter they used for their temperature measurements.

The input for first order model calculations is shown in Figure 5.

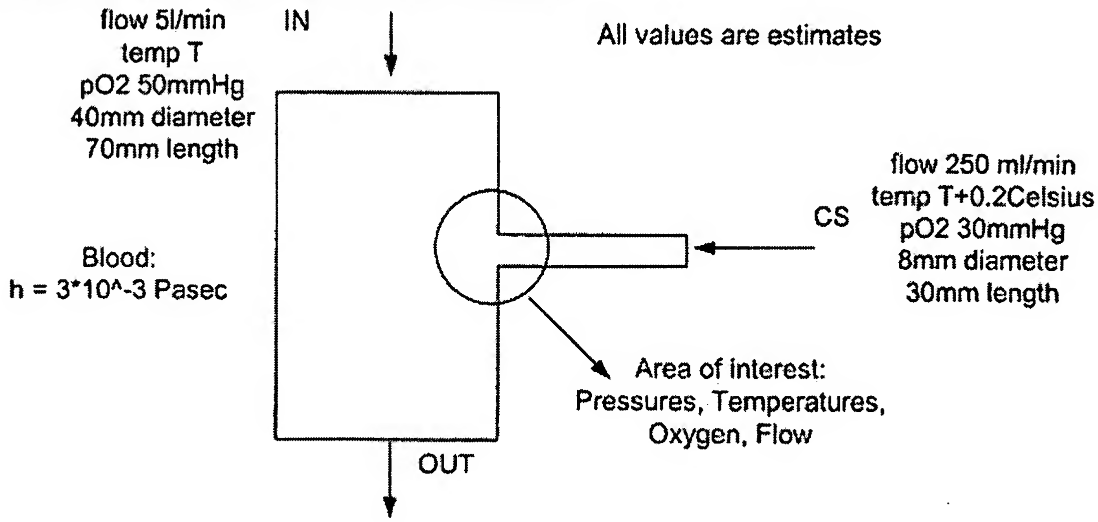


Figure 5 First order model of the flow from the coronary sinus into the right atrium.

The results of a steady flow calculation are shown in Figure 6 and Figure 7.

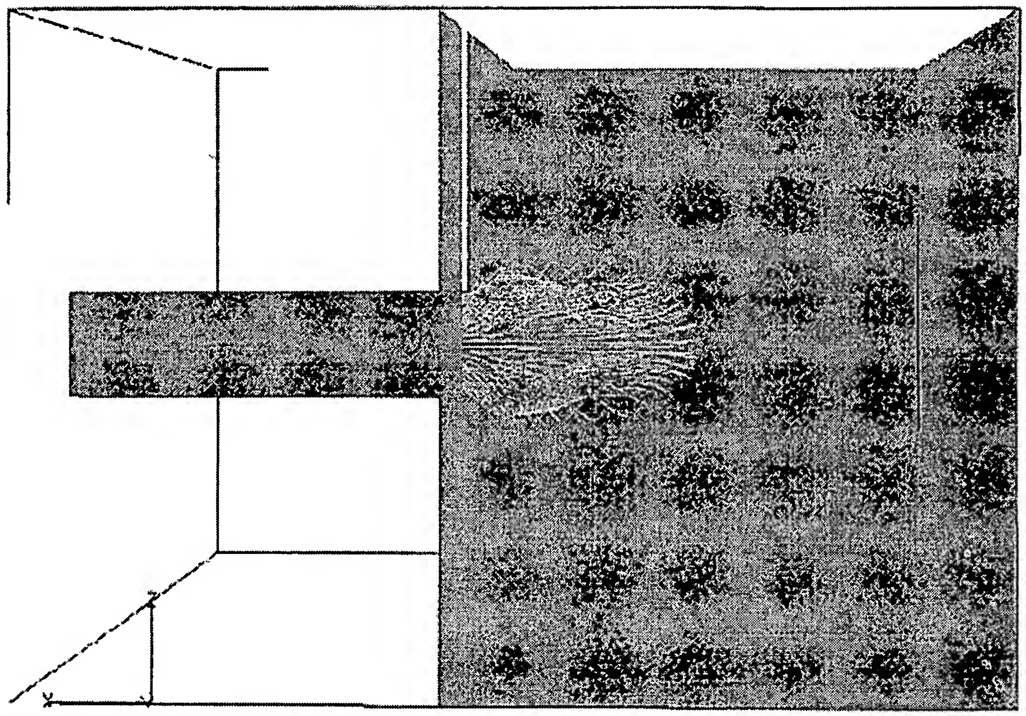


Figure 6 Streamlines (with velocity in color) in top view. Coronary Sinus blood is flowing in from the left, flow through the atrium is into the paper.

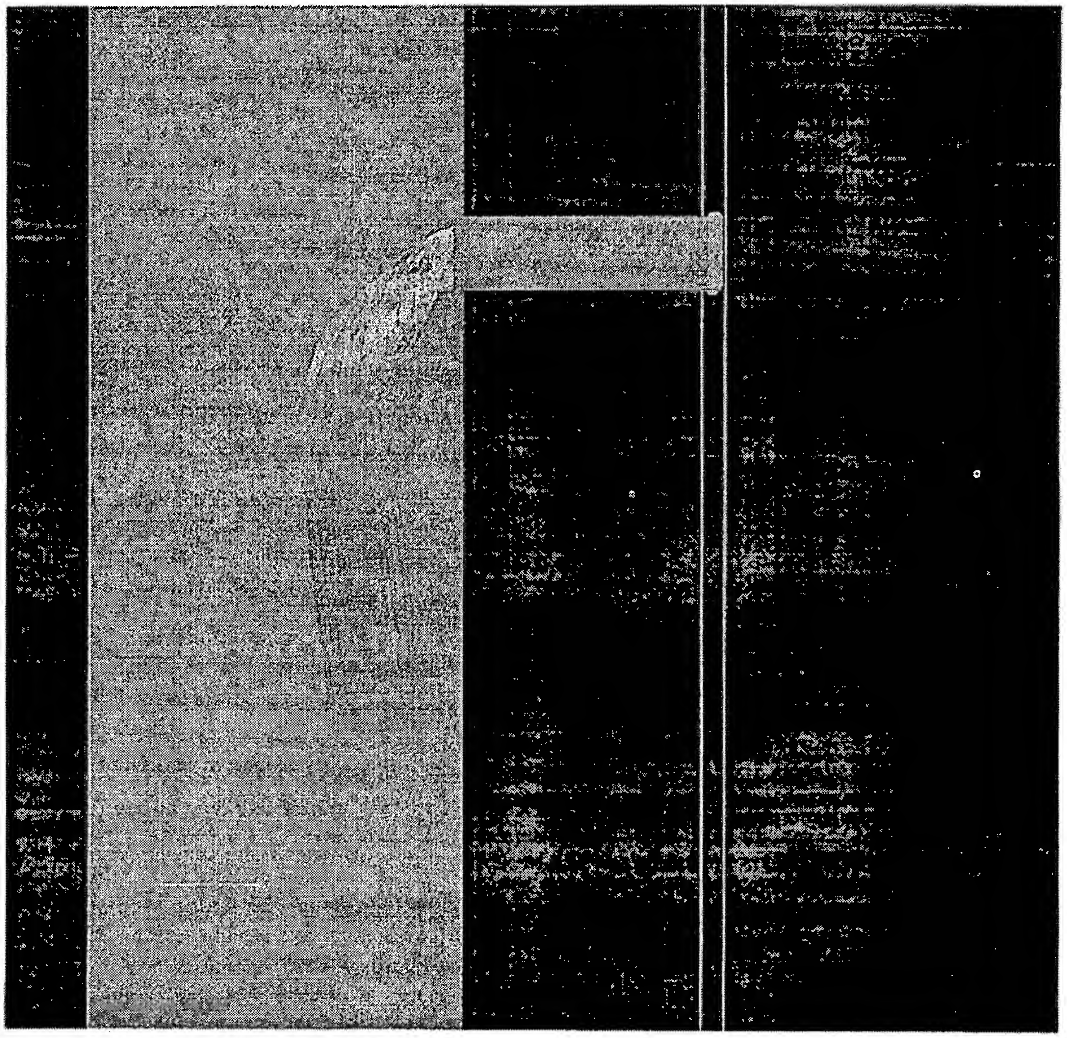


Figure 7 Side view of Figure 6. Coronary Sinus flow is coming from the right and atrial flow is top down.

These calculations are far from the reality of a beating heart. In this steady state flow it can be seen that the fluids don't mix and that the flow extends about 1 cm into the atrium. This means that also the properties stay unmixed. In a real situation this might be the case during a specific time in the heart cycle. These results serve as an indication for the spatial extent of the signal that we are looking for.

More complex models are possible{van de Vosse, Van Steenhoven, et al. 1990 382 /id}, but we have chosen to focus on the experiment.

From the considerations discussed above a first list of requirements for temperature measurements could be:

- Noise level 10m°C
- 2 sensors on catheter to be able to measure differentials
- Sample rate >5Hz
- Bandwidth 15Hz
- Catheter should be steerable

MATERIALS AND METHODS

Catheters

In collaboration with the Design and Build Laboratory (DBL) of the Bakken Research Center (BRC) a catheter containing three pressure sensors, three thermocouples and a tip electrode was made already for the original research of pressure signals (Figure 8).

Figure 8 Custom catheter. On the left the electrode tip is visible on the top of the picture. The electrode is connected to the outside via a coil. The pressure sensors are visible in the lumen in the tube. A thermocouple wire is mounted just in front of the pressure sensor (visible in picture on the right). The catheter can be manipulated with a stylet.

A standard Medtronic steerable ablation catheter with a thermocouple integrated in the tip was also used.

Data acquisition

The position of the tip electrode is visible on the Loca Lisa system. This positional information can be continuously recorded by a labview application using the serial communication port on the Loca Lisa system.

In the animal experiment done in Decem[redacted] Thermocouple voltage and ECG are acquired by the Porti-Dat portable system from Twente Medical Systems International using their software. No Cold Junction Compensation was done.

The animal experiment o[redacted]used a NI PCM-CIA card 435x and PSH32-TC6 accessory cable, specially for thermocouples, with automatic Cold Junction Compensation, but acquisition speed limited to about 1 sample per second.

In vitro setup.

Some experiments to determine the noise level on temperature sensors and the influence of the acquisition method on this were done and are described in the appendix.

The custom catheter in its form as described in paragraph 0 was tested in an aquarium containing a saline solution with Loca Lisa electrodes attached to it. Simultaneous temperature and position recording was tested.

A setup in an aquarium with slightly warmer water flowing in through a tube was done to check if the expected temperature differences are measurable.

In vivo setup

An experiment to measure the ECG, pressure, position and temperature simultaneously in a goat was proposed to the animal ethical committee[8] and approved. This experiment was done already in the context of the focus on pressure and further details are given in that report.

Two more animal experiments were done in the spare time of other experiments on animals.

Temperature recording only was done on a calf during an experiment of the Cardiac Surgery group of the University of Maastricht. A catheter was moved in and out of the coronary sinus with the help of X-ray and the temperature was recorded.

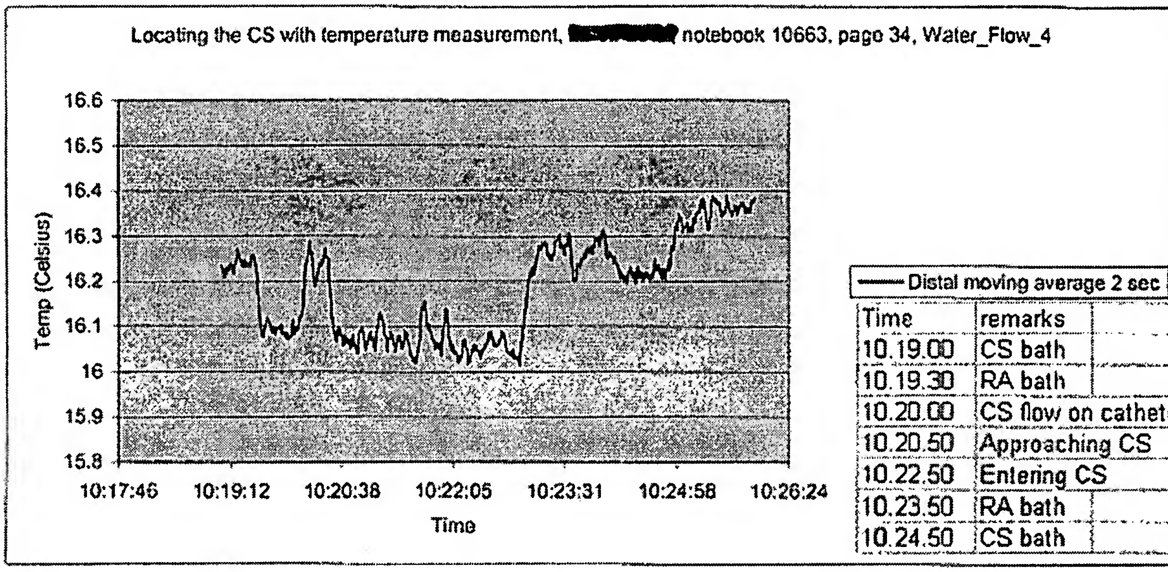
Combined position and temperature recordings were done on a dog during an experiment of the AM department of the BRC (Olaf Eick, Koen Michels). Loca Lisa electrodes are placed on the chest and a reference electrode is placed in the apex of the right ventricle. A vein is prepared for entry of a steerable catheter to map some points of the heart. During this while procedure the temperature and the position of the tip of the catheter are recorded.

RESULTS

In vitro

Results from the aquarium test showed that whole measurement setup allowing simultaneous recording of temperature and position was functioning properly.

Results from the simulation of the coronary sinus flow are shown in Figure 9.



Time	remarks
10.19.00	CS bath
10.19.30	RA bath
10.20.00	CS flow on catheter in R/
10.20.50	Approaching CS
10.22.50	Entering CS
10.23.50	RA bath
10.24.50	CS bath

Figure 9 Temperature recorded with custom catheter in water basin simulating the coronary blood flow

It can be seen that the temperature differences that are expected can be recorded with this setup.

In vivo

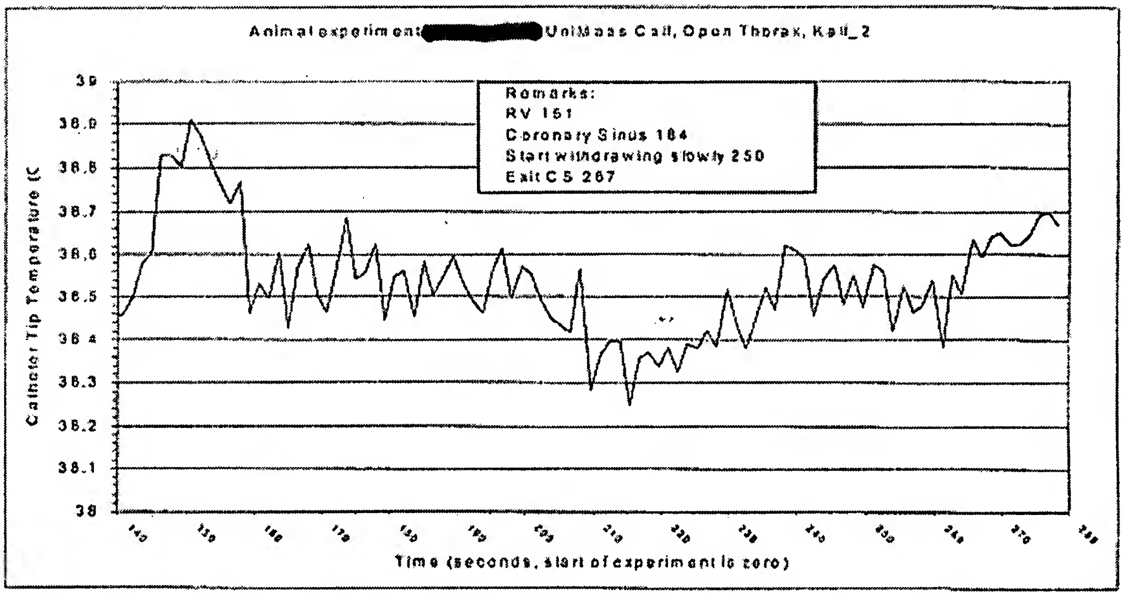


Figure 10 Temperature of the tip of the catheter as a function of time measured in a calf. The remarks show where the tip is at specific points in time. The noise level is rather big compared to the temperature differences. From t=184 to 250 the catheter is not moving and still there is a dip in the temperature. At the point were the catheter is exiting the coronary sinus the temperature is increasing. Both effects could be explained by the fact that this is measured with open thorax. Temperature differentials would not be disturbed by an overall change in temperature.

The experiment on a goat on Dec [redacted] had a focus on pressure. Still the temperature was also recorded.
Note that there was no cold junction correction done, so all temperature variations of the cold junction are superimposed on this data. Still the results were inspected to check if there is information in it despite this fact.
Looking back at the experiment two tests relevant for temperature were done. One recording (amongst others) the temperature and the ECG while withdrawing the catheter (geit_06, shown in Figure 11). The other one recording the ECG, temperature and Loca Lisa coordinates while withdrawing the catheter (geit_08, shown in Figure 12)

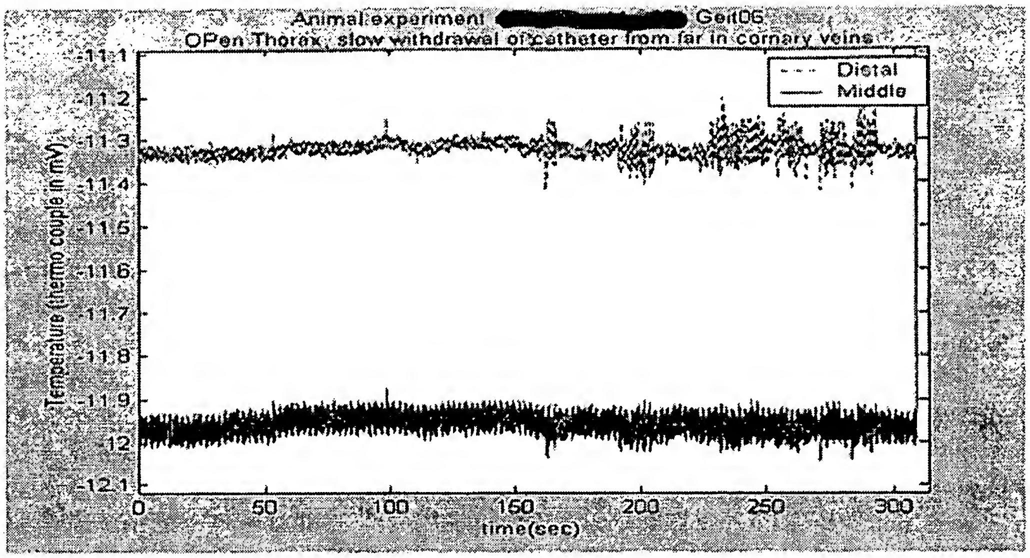


Figure 11 Temperature (in thermocouple mV) as function of time. At t = 34, 52 and 92 the catheter is withdrawn about 0.5cm. It was not noted if it was completely withdrawn from the CS (probably not). There is no clear rise or drop in temperature visible. The explanation might be the open thorax and no cold junction compensation.

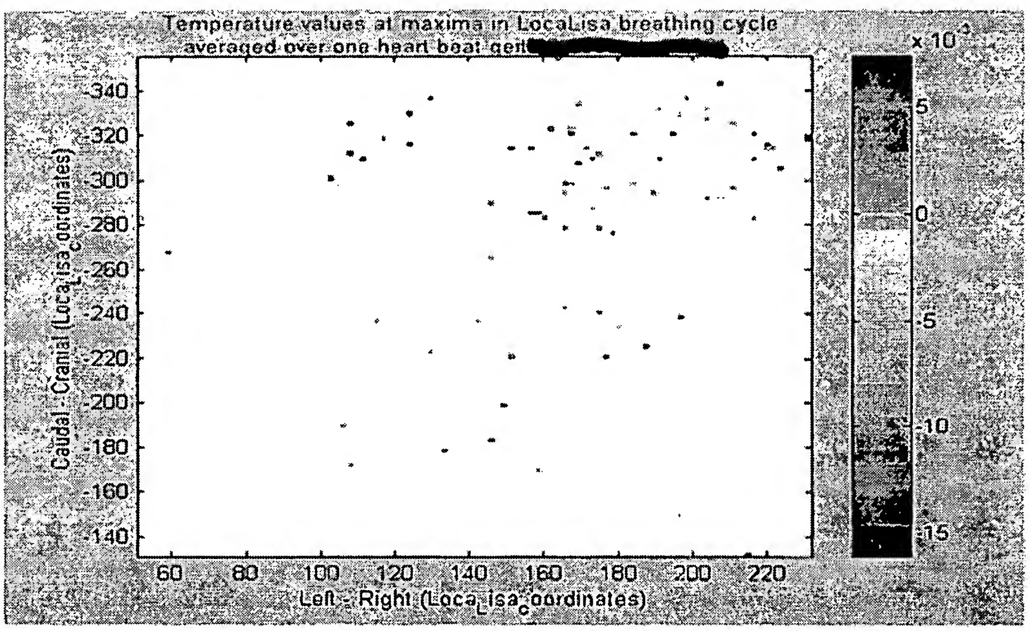


Figure 12 The catheter was slowly withdrawn from the coronary sinus. The position information fluctuates with the breathing cycle, only the maxima are taken into account. At this maximum the temperature values during one heart beat defined as the time between the two nearest R peaks in the ECG are taken into account and averaged. These values are plotted in color as a function of Left-Right and Caudal-Cranial

position. The colorscale representing the temperatures is in V (5mV corresponds to 0.1°C. If the warmer points are in the coronary sinus and the colder outside the coronary sinus is unclear from this experiment.

An individual temperature recording during one heart beat is given in Figure 13

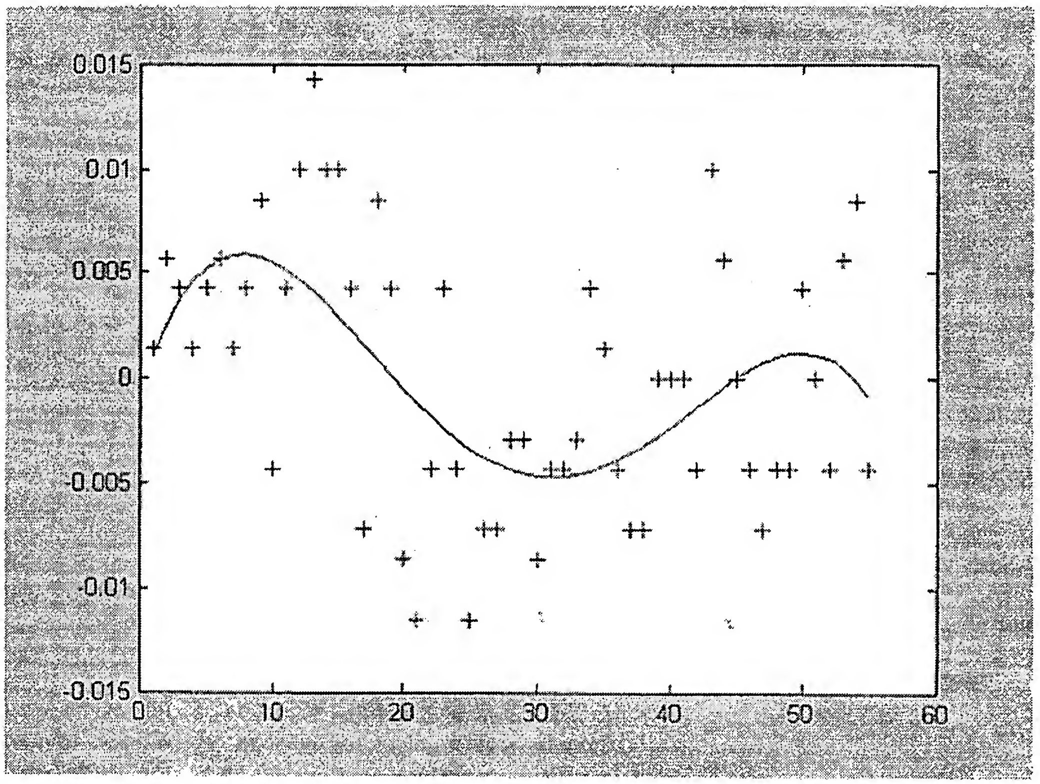


Figure 13 Temperature as a function of sample number (blue crosses). Temperature in V (thermocouple output). Sample rate 100 Hz. Green line is fourth order polynomial fit (least squares). These are the temperatures recorded between two R peaks in the ECG. This plot gives an idea about the kind of information that is available in this detail compared to the average that was shown in the previous figure. One can for example think of averaging a more specific time window in the ECG or attributing some other characteristic to this signal.

The experiment done on April 16 2002 on a dog had two successful trials, one with the mapping catheter and one with the custom catheter. The results will be described along with the figures below.

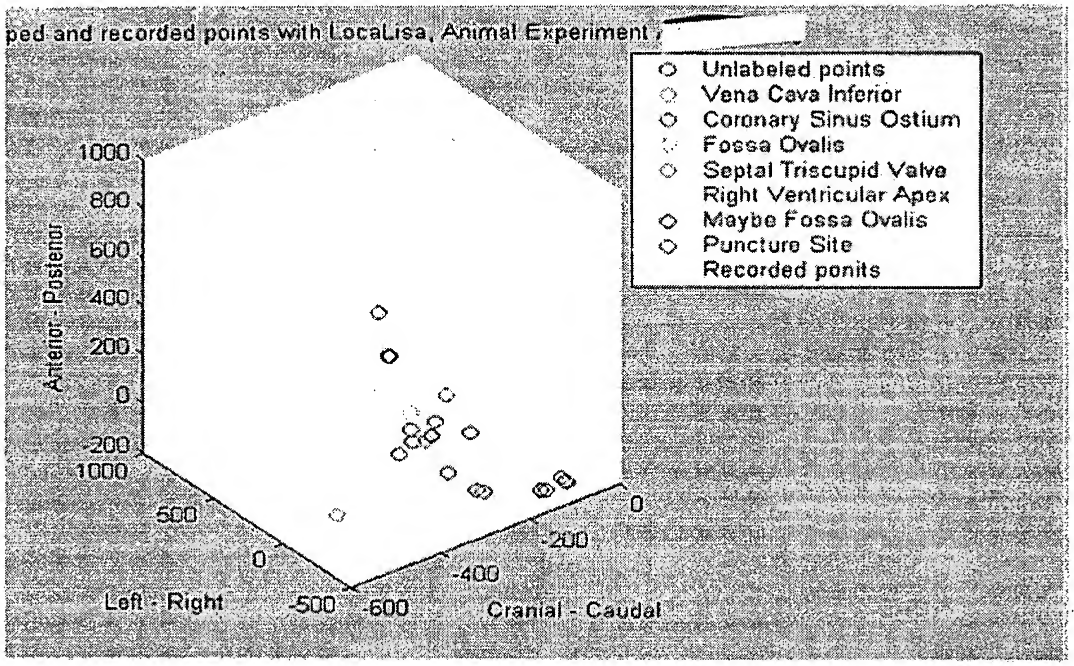


Figure 14 The physician can tell on the basis of X-ray and his experience where the tip of the catheter is. At this moment a point is mapped in the Loca Lisa system and labeled accordingly. This plot shows the mapped points in a 3D coordinate system (Loca Lisa units). The "tail" of unlabeled points towards the lower right side are all in the Coronary Sinus.

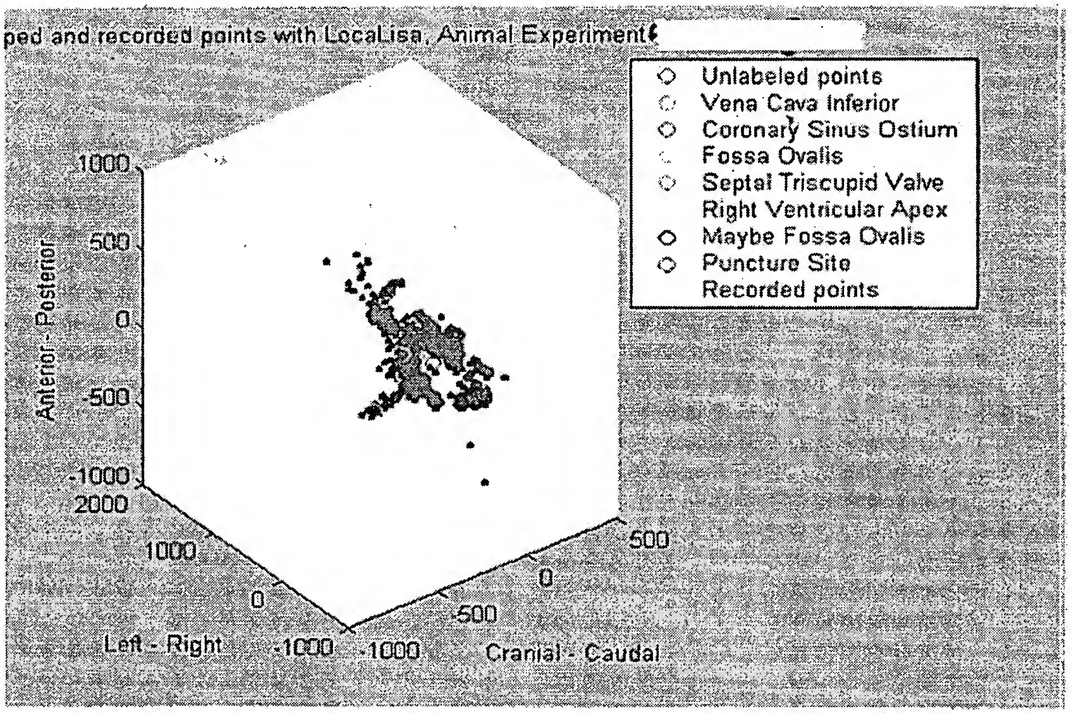
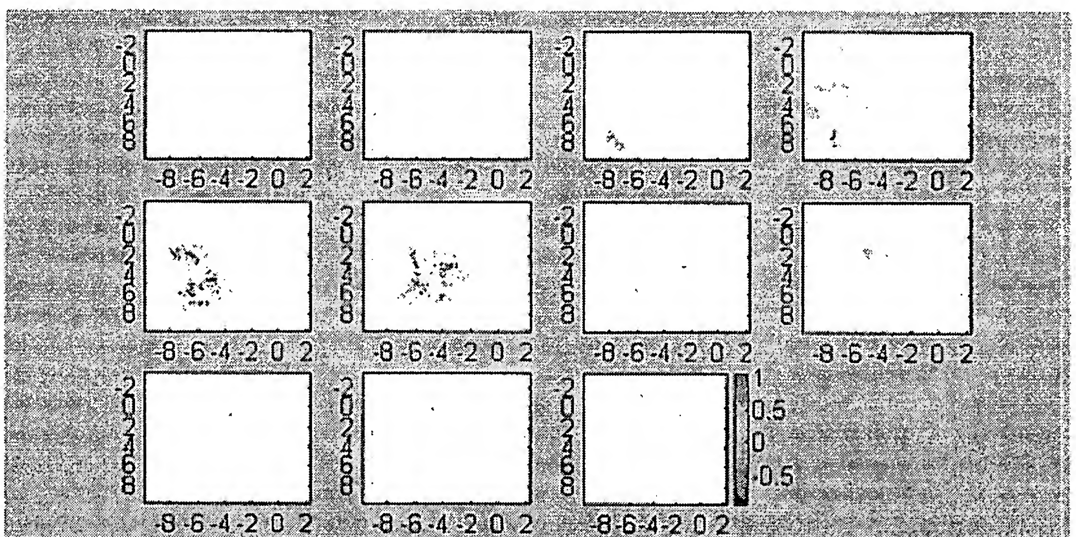


Figure 15 The continuously recorded points superimposed on the mapped points from the previous figure. It has to be mentioned that an offset was observed between the continuously recorded points (labview program) and the mapped points (Loca Lisa) that has been corrected after the measurements by translating the data over a constant vector. Via the mapped points there is a relation between the anatomy and the Loca Lisa coordinates. Each recorded point also has a temperature value.



Temperature in color for recorded points as function of Caudal-Cranial (vertical axis in cm) and Left -Right (horizontal axis in cm) Each plot represents a slice at a different position in Anterior - Posterior direction. Average removed from temperature. Multiple measurements at same position are removed.

Figure 16 See subscript on the plot. What can be seen from this plot is that the temperature differences are in the order of 1.5 °C, that is more then expected. The read tail are the points recorded in the coronary sinus, clearly warmer then the atrium. The next figure zooms in on the Coronary Sinus ostium. Note that Loca Lisa coordinates are transformed to cm using the calibration factors of the Loca Lisa system.

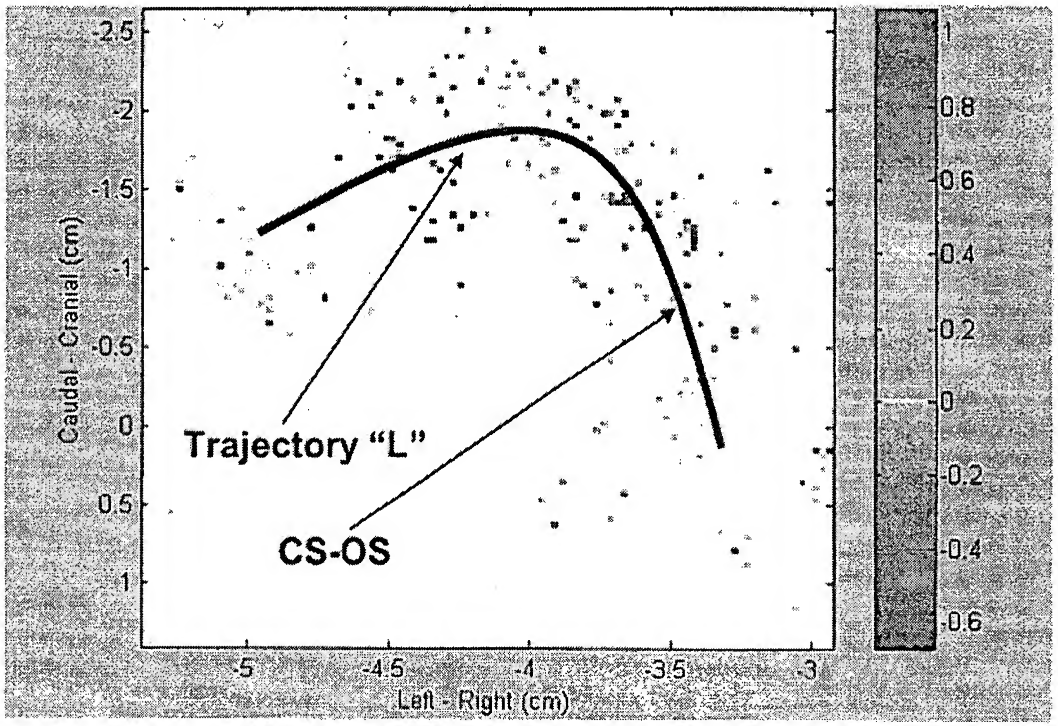


Figure 17 Same data as the previous figure but only points that are within about 1 cm of the labeled point CS-OS and the first two points inside the CS are plotted. All points in anterior-posterior position plotted in this plane (they are not further apart then 1 cm). Still the temperature difference is in the order of 1.6°C over these points only. It can be seen that the warmer points are in the coronary sinus and the colder points are around the ostium and outside of it in the atrium. The extent of the gradient will be in the order of 0.5cm estimated from this plot. Note that the spatial spread of the points is also due to spread in the Loca Lisa readings (for example due to breathing)

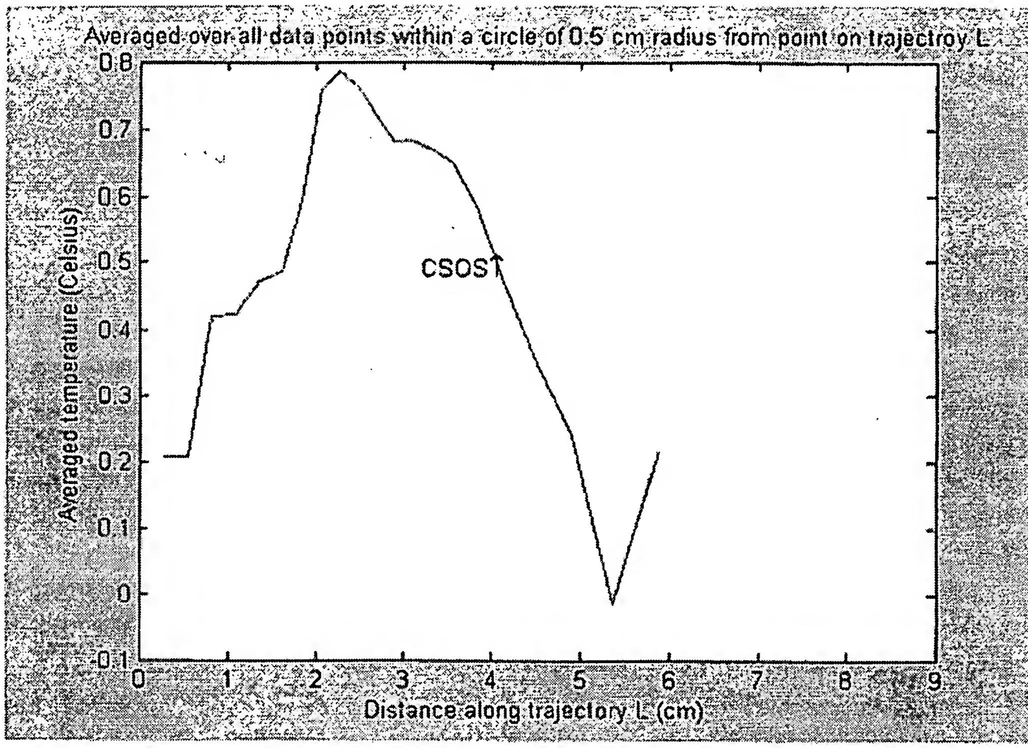


Figure 18 Temperature along the trajectory "L" of **Figure 17**. The temperature of each point on the traject was determined by averaging the temperatures of all data points within a range of 1 cm from that point. For this reason start and end temperatures should be interpreted carefully. The point marked as CSOS during the mapping is indicated with the arrow. There is a clear gradient in the temperature extending approximately 1 cm out of the CSOS.

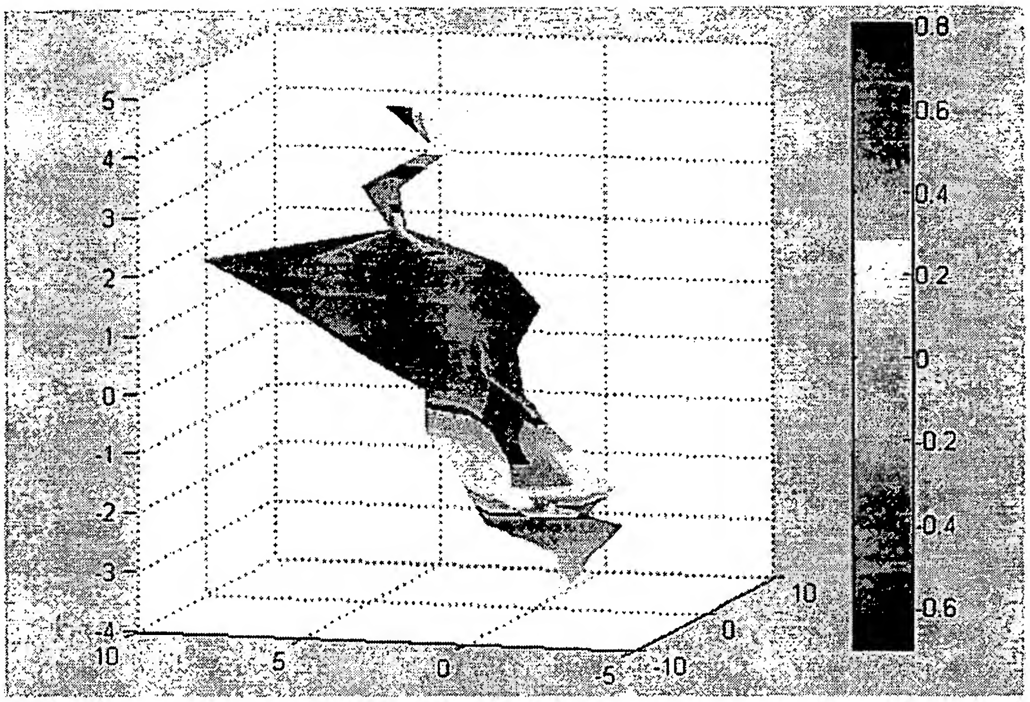
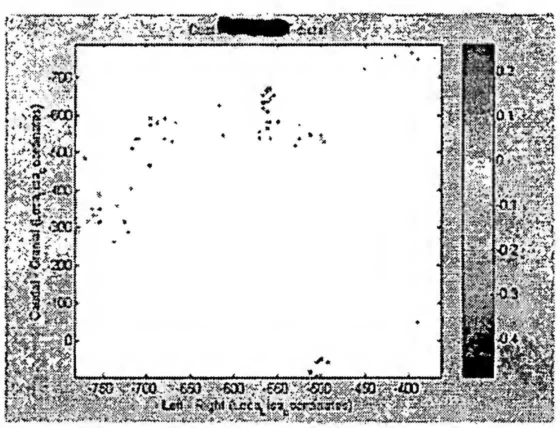
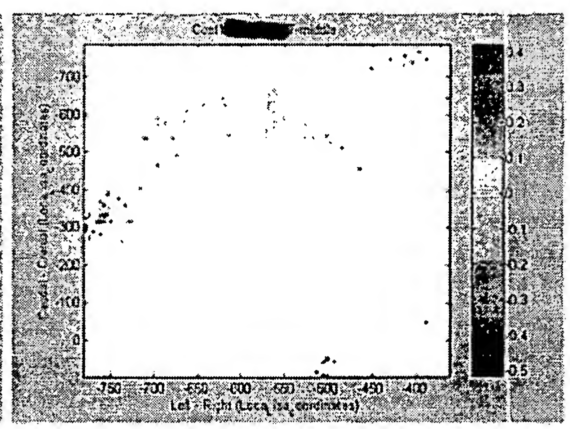


Figure 19 Temperature Anatomical map of the heart. This particular surface has been constructed by determining the contour of each slice shown in **Figure 16**. The temperature at a specific point on the surface was determined by averaging the temperatures of all data points within a range of 0.5 cm. If there were no data points the temperature was set to the average of that contour. The red spot is the coronary sinus.

The experiment with the custom catheter (with three thermocouples) can be analyzed in a similar way. During the recording the catheter was moved several times in and outside the coronary sinus. For comparison several points were recorded in the right atrium and right ventricle.





Medtronic Invention Disclosure Form

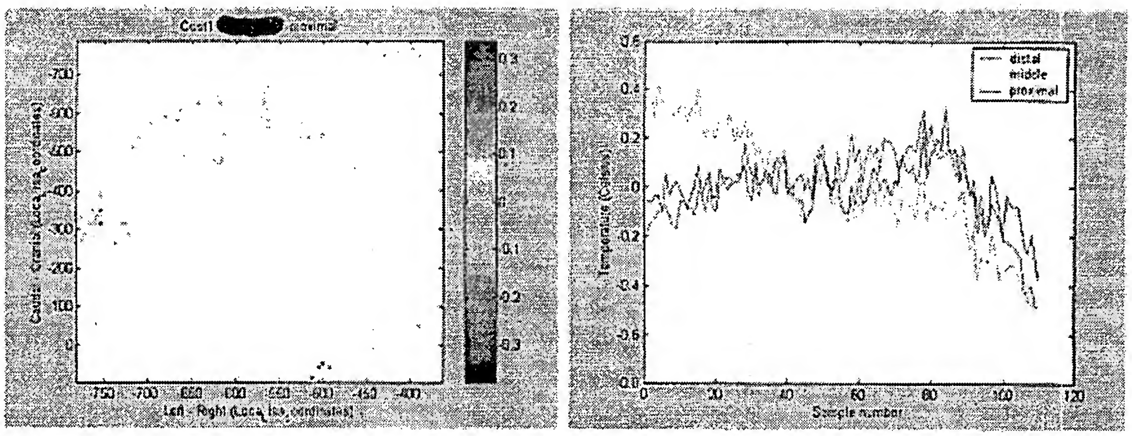


Figure 20 Upper Left: Distal temperature (in color) as a function of Left-Right and Caudal-Cranial. The colder points are in the right atrium and ventricle (group of dots right upper corner and in the middle below). Upper Right: Middle temperature. Note that the position information belongs to the tip, while the temperature is measured at the middle temperature sensor. It looks in this plot like the middle sensor has the maximum temperature far in the coronary sinus, while in reality it could already be measuring more towards the ostium were the real maximum is according to the distal temperatures (see text). Lower Left: Proximal temperatures are not as pronounced, maybe because it is already measuring in the atrium. Lower Right: Temperatures as a function of sample number.

Distance of the first thermocouple from the tip is 5mm, separation between following two sensors is 1cm. Changing from Loca Lisa coordinates to cm (with the calibration factor of 157) gives a distance of appr. 1.3 cm so the reasoning given above makes sense.

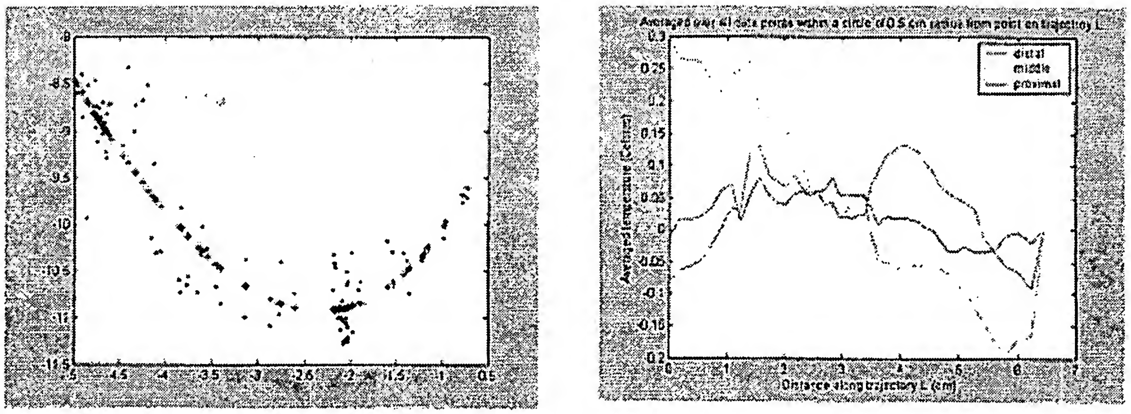


Figure 21 <u>Left:</u> Trajectory through the data points in the coronary sinus and just outside the coronary sinus. <u>Right:</u> Temperatures along this trajectory for all three sensors. The gradient around the CSOS is not so clear here, although this is the same animal. The curves do not exactly duplicate each other when translated to compensate for the distance between the sensors as argued before.

DISCUSSION

These measurements show that there is a temperature difference between the blood in the coronary sinus and the blood in the atrium of approximately 1°C. The spatial extent of the gradient is estimated at approximately 0.5cm around the ostium.

Main improvement for a follow up would be a higher sample rate of the temperature and synchronization with the ECG.

It might be possible to collect data from humans from standard ablation procedures with catheters with thermocouples, if temperature data can be recorded.

Keep in mind that for the final delivery system there will be no Loca Lisa, so the temperature recordings will have to do.

Sensors on the delivery system might be used to optimize the pacemaker system settings. The details are disclosed in an invention disclosure.

There are other possibilities that will be investigated and compared to this one:

[redacted]

CONCLUSION

These measurements give an indication that there is a temperature difference between the blood in the coronary sinus and the blood in the atrium of approximately 1°C. The spatial extent of the gradient is estimated at approximately 0.5cm around the ostium.

Main improvement for a follow up would be a higher sample rate of the temperature and synchronization with the ECG.

It might be possible to collect data from humans from standard ablation procedures with catheters with thermocouples, if temperature data can be recorded, or with the use of a testbox.

APPENDIX ThermoCouples

This appendix describes some measurements that were done to determine the noise level on temperature readings that are achievable with thermo couples and the influence of the acquisition method and thermocouple configuration on this.

Type of thermocouples:
All type T Copper Constantane
A)Pure thermocouple wire with a warm and a cold junction and voltage directly measured on copper wires.
B)Thermocouples inside custom catheter (cold junction somewhere in the grip)
C)Thermocouple inside ablation catheter (cold junction somewhere in the grip)

Acquisition method:
A)NI 435x PCM-CIA card with NI PSH32-TC6 accessory
B)Porti-dat from Twente Medical Systems
C)NI6024E PCMCIA card

[redacted]

REFERENCES

Reference List

1. Aggel,D.v., Shih,A. & Petersen-Stejskal,S. Comparison of InSync and InSync III Clinical Data.. 20th annual science & technology conference.
   Ref Type: Conference Proceeding

2. Kalvesten,E., Smith,L., Stemme,G. & Tenerz,L. The first surface micromachined pressure sensor for cardiovascular pressure. 574-579. 1998. IEEE 11th International Workshop on Micro Electro Mechanical Systems.
   Ref Type: Conference Proceeding

3. Millar,H.D. & Smith,R.A. Reduced catheter tip measurement device. Millar Instruments Inc. 08/744,478(US 5,902,248). 1999.
   Ref Type: Patent

4. Houben,R., Larik,V. & Receveur,R. Biomedical sensors for temporary and acute use. 2001.
   Ref Type: Pamphlet

5. Receveur,R. Coronary Sinus Lead Delivery System using Miniature Pressure Sensors as a means for Navigation. Medtronic Bakken Research Center.
   Ref Type: Report

6. Stewart,J.T. *et al.* Left ventricular energetics: heat production by the human heart. *Cardiovasc. Res.* 27, 1024-1032 (1993).

7. Hiles,M.C., Bourland,J.D., Wessale,J.L., Geddes,L.A. & Voorhees,W.D. Detection of ventricular tachycardia and fibrillation using coronary sinus blood temperature: a feasibility study. *Pacing Clin. Electrophysiol.* 16, 2266-2278 (1993).

8. Receveur,R., Michels,K., Feron,J. & Larik,V. LV Coronary Vein Lead Delivery, Canine study protocol for transvenous delivery system to the coronary sinus using pressure measurements as a guiding tool. 2001. Medtronic Bakken Research Center.
   Ref Type: Report